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Applicant : Masahiro HAMADA et al.
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Karin S. Lemack
Name of applicant, assignee, or Registered
Representative

[Signature]
Signature
March 4, 2008
Date

Sir:

DECLARATION UNDER 37 C.F.R. §1.132

I, Masahiro HAMADA, a citizen of Japan residing at 2-336, Kitabukuro-cho, Omiya-ku, Saitama-shi, Saitama 330-0835 Japan, hereby declare:

That I am currently a research scientist of Technology Development Group in the Functional Chemicals R&D Laboratories of the Research & Development Group of NIPPON KAYAKU KABUSHIKI KAISHA, and have been in that position since 2004;

That I hold a Master of Integrated Biosciences Degree in 2001 from University of Tokyo;

That I have reviewed the above-referenced patent application as well as the Office Actions, and I am familiar with its prosecution and the cited reference; and

That the following experiments were conducted by me or under my supervision, in order to prepare sulfomethylated

poly-ether sulfone by the following experiments according to (1) the thiourea method disclosed in cited reference WO 98/04598 (Kubota et al.) (for example, EXAMPLE 1 "Sulfonation of 4-Bromobutylstyrene Crosslinked Copolymer" of Kubota et al.), (2) the EtOCS₂K method disclosed in Kubota et al. (for example, EXAMPLE 2 "Sulfonation of 4-Bromobutoxymethylstyrene Crosslinked Copolymer" of Kubota), and determine an ion-exchange capacity of the obtained products.

(I) Experiments and results:

(1) Synthesis of sulfomethylated polyether sulfone by the thiourea method disclosed in Kubota

(i) Synthesis

After substituting the air inside of a 500 ml 4-neck flask with a stirrer, a thermometer, a reflux condenser, and a desiccant tube (containing calcium chloride in it) by nitrogen gas, 10.72 g of chloro-methylated poly-ether sulfone which was synthesized by the method described in the present Example 2, 100 ml of dimethyl sulfoxide and 4.11 g of thiourea were put into the flask, and stirred at 70 degrees Celsius for 4 hours.

After temperature in the reaction system became lower, reaction products were precipitated by adding dropwise the reactant solution into 500 ml of acetone, and the precipitate was separated by filtering. Separating process by washing the precipitate with acetone and filtering under reduced pressure was repeated, and then the obtained products were dried at 75 degrees Celsius. The product yield was 19.2 g. By Nuclear Magnetic Resonance (NMR) determination, the obtained products were identified that the products were the isothiuronium salt.

7.4 g of the obtained products were put into a 500 ml 4-neck flask with a stirrer, a thermometer, and a reflux condenser, and then 40 ml of hydrogen peroxide aqueous solution (34.5%) and 40 ml of water were added thereto, followed by stirring at 50 degrees Celsius for 6 hours for the reaction. Polymers were dispersed in hydrogen peroxide aqueous solution while the reaction. After temperature in

the reaction system becomes lower, a part of reaction products were separated by filtration. Washing it with water was repeated, and the obtained products were dried at 75 degrees Celsius. The yield of the products was 3.10 g. The residual reaction solution were stirred at 50 degrees Celsius for additional 6 hours (total 12 hours). Products were obtained as same procedure as described above. The yield of the products was 4.23 g.

(ii) Results

The products obtained in this experiment were identified by NMR determination. With regard to the product which reaction period is 6 hours, not only peaks which seem to be derived from sulfomethyl group (a chemical shift of 3.86 ppm), but a group of peaks which seems to be derived from isothiuronium salt (chemical shifts around 4.55ppm) was also found. With regard to 12 hours, both chemical shifts of sulfomethyl groups and isothiuronium salts were also found, too. By comparison of integrated peaks in the chart of the NMR determination, remaining rates of isothiuronium salts and conversion rates to sulfomethyl groups in the obtained products are estimated as follows:

Reaction period	Remaining rate of isothiuronium salts	Conversion rate to sulfomethyl group
6 hours	43%	57%
12 hours	24%	76%

It was confirmed that, in the reaction condition disclosed in Kubota, conversion rate to sulfomethyl group was only 57% and 43% remained in the form of isothiuronium salts. Furthermore, even two times of the reaction times disclosed in Kubota only showed conversion rates 76% and not 100%. We could not confirm whether the thiourea method disclosed in Kubota could convert chloro-methylated poly-ether sulfone to sulfomethylated poly-ether sulfone in

conversion rate 100% as shown in the present invention or not.

We tried to determine an ion-exchange capacity of the obtained polymers by the following methods.

(a) Direct titration method

(Direct titration method is a method that titrating a solution which solves a sample directly)

0.5 g of the obtained polymers were dissolved in 30 g of dimethyl sulfoxide at room temperature, and the solution was titrated with 0.1 N aqueous solution of potassium hydroxide. At the same time 0.1 N aqueous solution of potassium hydroxide was added dropwise into the solution, the solution become clouded little by little. As the titer of the alkaline solution become increased, turbidity of the solution become increased. With increase in turbidity, insoluble matters were precipitated on an electrode of the testing apparatus. Accordingly, we could not determine an ion-exchange capacity of the obtained polymers by the direct titration method.

(b) Immersing method

(Immersing method is a method that a sample is immersed in an alkaline solution, the immersed sample is removed from the alkaline solution after completion of ion-exchange, and then the alkaline solution is titrated)

Into an alkaline solution prepared by adding 5 ml of 0.1 N aqueous solution of sodium hydroxide to 40 ml of water, 0.3 g of the obtained polymers were added and immersed for 3 hours at room temperature. The immersed polymers were changed to oily products. It seems that was caused because the polymer absorbed water. To separate the products from the alkaline solution, we tried to filtrate it with filter paper. However, it was difficult to filtrate it because the filter paper was clogged. Accordingly, we could not determine an ion-exchange capacity of the obtained polymers by the thiourea method disclosed in Kubota by the immersing method although, if we could determine, the value might be 57% or 76% of that of the polymer of the present invention.

Further, in the above (i) method, the solution containing the obtained polymers became clouded and solid

products were precipitated. It seems that remained isothiuronium salt in polymer was decomposed by the titration with an alkaline and changed to an insoluble polymer.

Accordingly, the polymer containing remained isothiuronium salt in polymer can not use as the polymer for ion-exchange because the polymer changes to other polymer by an alkali such as potassium hydroxide even if the polymer contains sulfomethyl groups in the containing rate 57% or 76%.

(2) Synthesis of sulfomethylated polyether sulfone by the EtOCS_2K method disclosed in Kubota

(i) Synthesis

Into a 500 ml 4-neck flask with a stirrer, 10.23 g of chloro-methylated poly-ether sulfone which was synthesized by the method described in the present Example 2, 200 ml of ethanol and 10.72 g of O-ethyl potassium dithiocarbonate (EtOCS_2K) were put, and stirred at 70 degrees Celcius for 8 hours for the reaction. Polymers were dispersed in ethanol while the reaction. Then, the temperature in the reaction system was lowered to room temperature and the obtained products were separated by filtration, washed with water repeatedly and dried at 75 degrees Celcius, to obtain a yellow polymer.

Thus obtained yellow polymer were put into a 500 ml 4-neck flask with a stirrer, a thermometer and a reflux condenser, and then 100 ml of hydrogen peroxide solution (34.5%) were added thereto, followed by stirring at 50 degrees Celsius for 6 hours for the reaction. The obtained products were separated by filtration after the temperature in the reaction system was lowered to room temperature. It was washed with water repeatedly and dried at 75 degrees Celcius, and 12.04 of white polymer was obtained.

(ii) Results

In order to identify the obtained intermediate as yellow polymer, we tried to carry out NMR determination. However, NMR determination could not be performed because

the yellow polymer was not dissolved in any one of dimethyl sulfoxide, chloroform and N,N-dimethyl formamide. It seems that the chloromethyl group on the surface of the chloromethylated poly-ether sulfone caused cross-linking reaction in the presence of EtOCS₂K to produce cross-linked polyether sulfone which was insoluble to said solvents, among the reaction of chloro-methylated polyether sulfone and EtOCS₂K.

The obtained white polymer was immersed in 2 wt% diluted sulfonic acid over night, washed enough with ion-exchanged water, and then dried at 75 degrees Celsius to obtain the proton-exchanged resin. A certain amount of the resin was measured off and immersed in aqueous solution of 0.1N sodium hydroxide over night. After the resin was removed, remaining aqueous solution of sodium hydroxide was titrated with 0.1N HCl. The ion-exchange capacity of the obtained polymer was determined by the titer.

The measured ion-exchange capacity was 0.36 mmol/g (= meq/g) which is equal to 2778 g/mol as the equivalent weight of sulfonic acid group. The products obtained by the EtOCS₂K method disclosed in Kubota did not show sufficient ion-exchange ability. The present sulfomethylated polyether sulfone had 1.29 meq/g of the ion-exchange capacity shown in page 19, line 11-13 of the present English specification.

As same as the yellow polymer described above, NMR determination of the white polymer could not be performed because the white polymer was not dissolved in any one of dimethyl sulfoxide, chloroform and N,N-dimethyl formamide.

(II) Consideration:

As far as our experiments mentioned above, the thiourea method disclosed in Kubota et al. could convert only 57% and 76% of isothiuronium salts in polyether sulfone to sulfomethyl groups in sulfonation reaction time 6 hours and 12 hours, respectively, and isothiuronium salts were still remaining 43% and 24% in each obtained polymer. The polymer containing remained isothiuronium salt in polymer would have only insufficient ion-exchange capacity even if we could determine it because of insufficient conversion rate of

isothiuronium salts to sulfomethyl groups and, further, the obtained polymer could not use as a polymer for ion-exchange because of decomposition of remained isothiuronium salt in polymer with an alkaline as mentioned above.

Further, the results mentioned above suggest that very long times would be needed for the completion of the reaction because in the first six hours the reaction proceeded to 57%, but, in the second six hours, it proceeded only 19%, and this means that, in the second six hours, the reaction velocity was very slowdown and that, in more high reaction rate, the reaction velocity was more slowdown.

With respect to the EtOCS_2K method disclosed in Kubota et al., we could prepare only an insoluble polymer having insufficient ion-exchange capacity of 0.36 mmol/g (2778 g/mol as the equivalent weight of sulfonic acid group). It might be sulfomethylated poly-ether sulfone having only few sulfomethyl groups. However, we could not identify it because of the insoluble polymer.

Furthermore, Kubota discloses the method introducing sulfone group into polymers by using sodium sulfite as Method (4) (Column 7, line 12 to 15 in Kubota). However, by said method, chloromethyl group in the polyether sulfone had scarcely been reacted and scarcely changed into sulfomethyl group and the obtained products had scarcely ion-exchange capacities as shown in Comparative Example 2 in the present specification (see, page 21, last line to page 22, line 12 in the present English specification).

In the method of the present invention, the each conversion of chloromethyl groups in polyether sulfone into acetylthiomethyl groups and further the acetylthiomethyl groups into sulfomethyl group is 100% in the reaction time 8 hours and cross-linking reaction did not occurred such as the EtOCS_2K method. Said 100% of each conversion was confirmed by NMR determination in each reaction processes of the present Example 2 as follows;

In the present Example 2, after completion of the reaction of chloromethylated poly-ether sulfone to acetylthio-methylated poly-ether sulfone, the peak of 4.8 ppm which represents the chemical shift of methylene proton

in chloromethylated poly-ether sulfone was disappeared entirely, and the peak of 4.1 ppm which represents the chemical shift of methylene proton in acetylthio-methylated poly-ether sulfone was newly found with equal strength to the peak of said 4.8 ppm. Further, after completion of the next reaction of the acetylthio-methylated poly-ether sulfone to sulfomethylated poly-ether sulfone, the peak of 4.1 ppm was disappeared entirely, and the peak of 3.8 ppm which represents the chemical shift of methylene proton in sulfomethylated poly-ether sulfone was newly found with equal strength to the peak of said 4.1 ppm.

The facts mentioned above show that the chloromethyl groups in the chloromethylated poly-ether sulfone were entirely converted into the acetylthiomethyl groups, and then the acetylthiomethyl groups were entirely converted into the sulfomethyl groups after the said reactions. However, the yield of the obtained sulfomethylated polyether-sulfone from the chloromethylated polyether-sulfone in the present Example 2 was not 100% but about 92% as described in the present specification page 19 lines 8-9 because of loss of the polymer in the separation processes and so on.

Further, the sulfomethylated poly-ether sulfone obtained in the present invention has very high ion-exchange capacity, for example, in the present Example 2, it was 1.29 meq/g (770 g/mol as the equivalent weight of sulfonic acid group) (the present specification, page 19, line 11-13).

Considering the said Experimental results in polyether sulfone by the methods (1) and (2) specifically disclosed in Kubota, Kubota never discloses or suggests that, in polyether sulfone, only the method where chloromethyl groups were changed into sulfomethyl group through acetylthiomethyl group can obtain sulfomethylated polyether sulfone having very high ion-exchange capacity (1.29meq/g) in high yield(92%)(conversion rate 100% of chloromethyl groups into sulfomethyl group) by acetylthiolation at roomtemperature for 1 hour and sulfomethylation at 70 °C for 8 hours.

I further declare that all statements made herein of my own knowledge are true and that all statements made upon information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 101 of Title 18 of the United States Code and that such willful false statement may jeopardize the validity of the above identified application or any patent issuing thereon.

Masahiro Hamada

Masahiro HAMADA

February 28, 2008.

Date